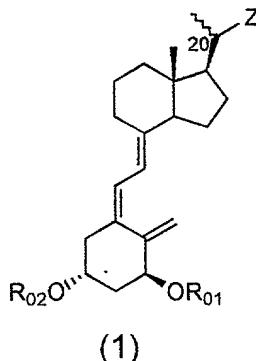


CLAIMS

1. A vitamin D₃ derivative expressed by the following general formula (1) or pharmaceutically permissible solvates thereof,

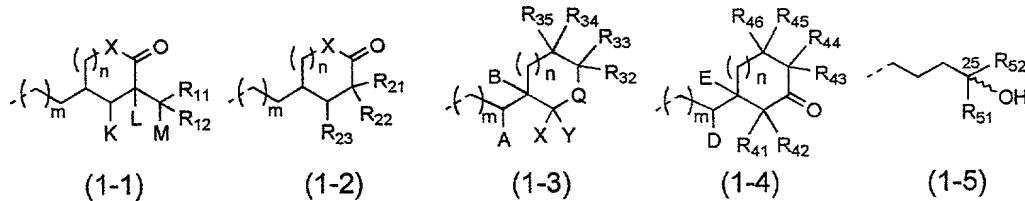
5



(1)

{wherein, R₀₁ and R₀₂ are each independently a hydrogen atom, a trimethylsilyl group, a triethylsilyl group, a t-butyldimethylsilyl group, an acetyl group, a methoxymethyl group or a tetrahydro-4H-pyran-2-yl group;

10 Z is one out of the following formulae (1-1), (1-2), (1-3), (1-4) or (1-5),



[in the above formulae (1-1) to (1-5),

15 m is an integer of 0 to 2;

n is an integer of 0 to 2;

X' is an oxygen atom or NH;

R₁₁ and R₁₂ are identical to or different from each other, and express a hydrogen atom or a C₁-C₄ alkyl group;

20 K, L and M take each a hydrogen atom; M is a hydrogen atom, and K and L together express a single bond and express a double bond in cooperation with the single bond already shown in the formula; or K is a hydrogen atom, and L and M together express a single bond and express a

double bond in cooperation with the single bond already shown in the formula:

R₂₁, R₂₂ and R₂₃ are identical to or different from each other, and they are a hydrogen atom, a hydroxy group, a carboxyl group, a trifluoromethyl group, a pentafluoroethyl group, a C₁-C₄ alkyloxycarbonyl group, a C₂-C₅ acyloxy group, a C₁-C₄ alkyloxy group or a C₁-C₄ alkyl group which may be substituted with a hydroxyl group, a C₂-C₅ acyloxy group or a C₁-C₄ alkyloxy group, or R₂₁ and R₂₂ together may express a C₃-C₆ cyclic alkyl group in cooperation with the carbon atom to which they are bonded;

Q expresses >C(-F)-R₃₁ or >N-R₃₁, and herein R₃₁ is a hydrogen atom, a hydroxyl group, a trifluoromethyl group, a pentafluoroethyl group, a C₂-C₅ acyloxy group, a C₁-C₄ alkyloxy group or a C₁-C₄ alkyl group which may be substituted with a hydroxyl group, a C₂-C₅ acyloxy group or a C₁-C₄ alkyloxy group;

R₃₂, R₃₃, R₃₄ and R₃₅ are identical to or different from each other, and they are a hydrogen atom, a hydroxyl group, a C₁-C₄ alkyl group or a C₂-C₅ acyloxy group;

A and B are identical to or different from each other, and they express a hydrogen atom or a hydroxyl group, or together express a single bond and form a double bond in cooperation with the single bond already shown in the formula;

X and Y together express a carbonyl group in cooperation with the carbon atom to which they are bonded, one of them is a hydrogen atom and the other is a hydroxyl group, or one of them is a hydrogen atom and the other is a C₂-C₅ acyloxy group;

R₄₁ and R₄₂ are identical to or different from each other, and they express a hydrogen atom, a hydroxyl group, a trifluoromethyl group, a pentafluoroethyl group, a C₂-C₅ acyloxy group, a C₁-C₄ alkyloxy group or a C₁-C₄ alkyl group which may be substituted with a hydroxyl group, a C₂-C₅ acyloxy group or a C₁-C₄ alkyloxy group, or both the members together express a C₁-C₅ alkylidene group, or they express a C₃-C₆ cyclic alkyl group in cooperation with the carbon atom to which they are bonded;

R₄₃ and R₄₄ are identical to or different from each other, and they express a hydrogen atom, a hydroxyl group, a trifluoromethyl group, a

5 pentafluoroethyl group, a C₂-C₅ acyloxy group, a C₁-C₄ alkyloxy group or a C₁-C₄ alkyl group which may be substituted with a hydroxyl group, a C₂-C₅ acyloxy group or a C₁-C₄ alkyloxy group, or both the members together express a C₁-C₅ alkylidene group, or express a C₃-C₆ cyclic alkyl group in cooperation with the carbon atom to which they are bonded;

10 R₄₅ and R₄₆ are identical to or different from each other, and they express a hydrogen atom, a hydroxyl group, a trifluoromethyl group, a pentafluoroethyl group, a C₂-C₅ acyloxy group, a C₁-C₄ alkyloxy group or a C₁-C₄ alkyl group which may be substituted with a hydroxyl group, a C₂-C₅ acyloxy group or a C₁-C₄ alkyloxy group;

15 D and E express each a hydrogen atom, D is a hydroxy group and E expresses a hydrogen atom; D and E together express a single bond and express a double bond in cooperation with the single bond already shown in the formula, or E and R₄₁ together express a single bond and express a double bond in cooperation with the single bond already shown in the formula, wherein D expresses a hydrogen atom or a hydroxy group; and R₄₂ expresses a hydrogen atom, a hydroxyl group, a trifluoromethyl group, a pentafluoroethyl group, a C₂-C₅ acyloxy group, a C₁-C₄ alkyloxy group or a C₁-C₄ alkyl group which may be substituted with a hydroxyl group, a C₂-C₅ acyloxy group or a C₁-C₄ alkyloxy group;

20 R₅₁ expresses -CONR₅₁₁R₅₁₂, -COR₅₁₃ or -C(OH)R₅₁₄R₅₁₅, wherein R₅₁₁ and R₅₁₂ are identical to or different from each other, and they are a hydrogen atom or a C₁-C₄ alkyl group, or both the members together express a nitrogen-containing C₃-C₈ alkyl ring or a morpholino group in cooperation with the nitrogen atom to which they are bonded; and R₅₁₃, R₅₁₄ and R₅₁₅ are identical to or different from each other, and they express a C₁-C₄ alkyl group;

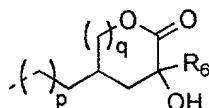
25 R₅₂ expresses a methyl group, an ethyl group, a trifluoromethyl group or a pentafluoroethyl group,

30 with the proviso that the following compounds (a), (b) and (c) are excluded,

(a) a compound in which the groups of one combination out of R₂₁ and R₂₂, R₃₂ and R₃₃, R₃₄ and R₃₅, R₄₁ and R₄₂, R₄₃ and R₄₄, and R₄₅ and R₄₆ are both hydroxy groups, both alkyloxy groups, or a hydroxy group and an

alkyloxy group,

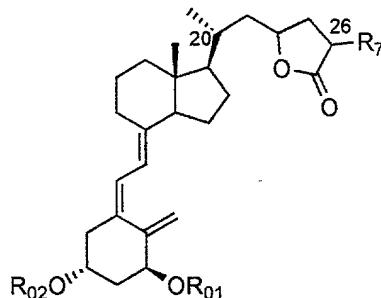
(b) a compound expressed by the above formula (1) in which Z is the following formula (1-6),



(1-6)

5 (wherein, p and q are each 0 or the integer 1; R₆ is a hydrogen atom or a C₁-C₄ alkyl group), and

(c) a compound of the following formula (2),



(2)

10 (wherein, R₀₁ and R₀₂ are defined in the same manner as in the above formula (1); the configuration of the carbon atom at the 20-position is (R)-configuration; R₇ is a methyl group or a methylene group; when R₇ is a methylene group, the bond between R₇ and the carbon atom at the 26-position is double bond).

15 2. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 1, wherein, in the above formula (1), Z is one out of (1-2), (1-3), (1-4) and (1-5).

3. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 1, wherein, in the above formula (1), Z is (1-1).

20 4. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 1, wherein, in the above formula (1), Z is (1-2).

5. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 1, wherein, in the above formula (1), Z is (1-3).

6. A vitamin D₃ derivative or a pharmaceutically permissible
5 solvate thereof described in Claim 1, wherein, in the above formula (1), Z is (1-4).

7. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 1, wherein, in the above formula (1), Z is (1-5).

10 8. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in one out of Claims 1 to 7, wherein, in the above formula (1), R₀₁ and R₀₂ are both hydrogen atoms.

9. A vitamin D₃ derivative or a pharmaceutically permissible
15 solvate thereof described in one out of Claims 1 to 6, wherein, in the above formula (1), m is 0 or 1.

10. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in one out of Claims 1 to 6, wherein, in the above formula (1), n is 0 or 1.

11. A vitamin D₃ derivative or a pharmaceutically permissible
20 solvate thereof described in Claim 3 or 4, wherein, in the above formula (1), X' is an oxygen atom.

12. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 3, wherein, in the above formula (1), R₁₁ and R₁₂ are identical to or different from each other, and they are a hydrogen
25 atom, a methyl group or an ethyl group.

13. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 3, wherein, in the above formula (1), K is a hydrogen atom, and L and M together express a single bond and express a double bond in cooperation with the single bond already shown in the
30 formula.

14. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 4, wherein, in the above formula (1), R₂₁ and R₂₂ are identical to or different from each other, and they are a hydrogen atom, a hydroxy group or a C₁-C₄ alkyl group, or R₂₁ and R₂₂ together express

a C₃-C₆ cyclic alkyl group in cooperation with the carbon atom to which they are bonded.

15. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 4, wherein, in the above formula (1), R₂₃ is 5 a hydrogen atom or a hydroxyl group.

16. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 4, wherein, in the above formula (1), the combination of R₂₁, R₂₂ and R₂₃ is one out of

- (a) R₂₁, R₂₂ and R₂₃ are all hydrogen atoms,
- 10 (b) R₂₁ and R₂₂ are methyl groups, and R₂₃ is a hydrogen atom,
- (c) the combination of R₂₁ and R₂₂ is a methyl group and a hydroxyl group, and R₂₃ is a hydrogen atom,
- (d) the combination of R₂₁ and R₂₂ is a methyl group and a hydroxyl group, and R₂₃ is a hydroxyl group and
- 15 (e) R₂₁ and R₂₂ together form a cyclopropyl group in cooperation with the carbon atom to which they are bonded, and R₂₃ is a hydrogen atom.

17. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 5, wherein, in the above formula (1), Q is >C(-F)-R₃₁.

20 18. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 5, wherein, in the above formula (1), Q is >N-R₃₁.

25 19. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 5, wherein, in the above formula (1), R₃₁ is a hydrogen atom, a hydroxyl group or a C₁-C₄ alkyl group which may be substituted with a hydroxy group, a C₂-C₅ acyloxy group or a C₁-C₄ alkyloxy group.

30 20. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 5, wherein, in the above formula (1), R₃₂, R₃₃, R₃₄ and R₃₅ are each a hydrogen atom.

21. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 5, wherein, in the above formula (1), A and B are both hydrogen atoms, A is a hydroxyl group and B is a hydrogen atom, or A and B together express a single bond and form a double bond in

cooperation with the single bond already shown in the formula.

22. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 5, wherein, in the above formula (1), X and Y together express a carbonyl group in cooperation with the carbon atom to which they are bonded.

5 23. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 6, wherein, in the above formula (1), R₄₁ and R₄₂ are both hydrogen atoms or together express a methylene group.

10 24. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 6, wherein, in the above formula (1), R₄₃ and R₄₄ are both hydrogen atoms or together express a methylene group.

25. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 6, wherein, in the above formula (1), R₄₅ and R₄₆ are both hydrogen atoms.

15 26. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 6, wherein, in the above formula (1), D and E are both hydrogen atoms, D and E together express a single bond and form a double bond in cooperation with the single bond already shown in the formula, or D is a hydrogen atom and E and R₄₁ together express a single bond 20 and express a double bond in cooperation with the single bond already shown in the formula.

27. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 7, wherein, in the above formula (1), R₅₁ is -CONR₅₁₁R₅₁₂ or -COR₅₁₃.

25 28. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 7, wherein, in the above formula (1), R₅₁ is -CONR₅₁₁R₅₁₂

29. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 7, wherein, in the above formula (1), R₅₁ is 30 -COR₅₁₃.

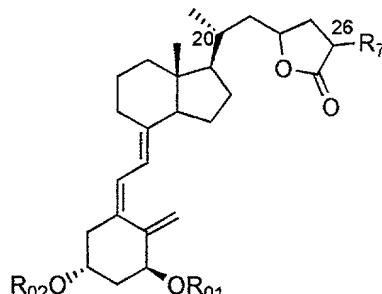
30. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 7, wherein, in the above formula (1), R₅₁ is -CONR₅₁₁R₅₁₂, and R₅₁₁ and R₅₁₂ are identical to or different from each other, and they are a methyl group or an ethyl group, or both the members together

express an aziridine, pyrrolidine, piperidine or morpholino ring in cooperation with the nitrogen atom to which they are bonded.

31. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 7, wherein, in the above formula (1), R₅₁ is 5 -COR₅₁₃, and R₅₁₃ is a methyl group or an ethyl group.

32. A vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in Claim 7, wherein, in the above formula (1), R₅₂ is a methyl group.

33. A treating agent for an inflammatory respiratory disease 10 containing a therapeutically effective amount of a vitamin D₃ derivative described by the following general formula (3) or pharmaceutically permissible solvate thereof,



15

(in the formula, R₀₁, R₀₂ and R₇ are defined in the same manner as in the above formula (2)).

34. A treating agent for an inflammatory respiratory disease containing a therapeutically effective amount of a vitamin D₃ derivative or a 20 pharmaceutically permissible solvate thereof described by one out of Claims 1 to 32.

35. A treating agent for an inflammatory respiratory disease described in Claim 33 or 34, wherein the inflammatory respiratory disease is one or not less than two kinds of inflammatory respiratory diseases selected 25 from a group consisting of acute upper airway infection, chronic sinusitis, allergic rhinitis, chronic lower airway infection, pulmonary emphysema, pneumonia, bronchial asthma, tuberculosis sequela, acute respiratory

distress syndrome, cystic fibrosis and pulmonary fibrosis.

36. A treating agent for an inflammatory respiratory disease described in Claim 35, wherein the acute upper airway infection is one or not less than two kinds of diseases selected from a group consisting of common cold, acute pharyngitis, acute rhinitis, acute sinusitis, acute tonsillitis, acute pharyngitis, acute epiglottitis and acute bronchitis.

5 37. A treating agent for an inflammatory respiratory disease described in Claim 35, wherein the chronic lower airway infection is one or not less than two kinds of diseases selected from a group consisting of chronic 10 bronchitis, diffuse panbronchiolitis and bronchiectasis.

15 38. A treating agent for one or not less than two kinds of inflammatory respiratory diseases selected from a group consisting of chronic bronchitis, diffuse panbronchiolitis, bronchiectasis, bronchial asthma, pulmonary emphysema, tuberculosis sequela and cystic fibrosis which contains a therapeutically effective amount of a vitamin D₃ derivative or pharmaceutically permissible solvate thereof described in one out of Claims 1 to 32.

20 39. A treating agent for a disease selected from a group consisting of malignant tumors, rheumatoid arthritis, osteoporosis, diabetes mellitus, hypertension, alopecia, acne, psoriasis and dermatitis which contains a therapeutically effective amount of a vitamin D₃ derivative or pharmaceutically permissible solvate thereof described in one out of Claims 1 to 32.

25 40. A compound having vitamin D₃ antagonistic effect which is a vitamin D₃ derivative or a pharmaceutically permissible solvate thereof described in one out of Claims 2, 4 to 11, and 14 to 32.

41. A treating agent for hypercalcemia attributable to vitamin D excess which contains a therapeutically effective amount of a compound described in Claim 40.

30 42. A treating agent for hypoparathyroidism which contains a therapeutically effective amount of a compound described in Claim 40.

43. A treating agent for metabolic disorder of cartilage which contains a therapeutically effective amount of a compound described in Claim 40.

RECORDED IN U.S. PATENT AND TRADEMARK OFFICE

44. A pharmaceutical composition composed of a vitamin D₃ derivative or pharmaceutically permissible solvate thereof described in one out of Claims 1 to 32, and a pharmaceutically permissible carrier.